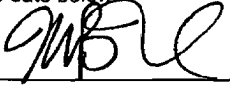


# **EXHIBIT A**

CERTIFICATE OF MAILING 37 C.F.R. 1.8	
I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-01450, on the date below:	
March 10, 2005 Date	 Mark B. Wilson

**PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:  
JOHNSTON ET AL.

Serial No.: 10/023,437

Filed: DECEMBER 17, 2001

For: METHODS AND COMPOSITIONS FOR  
VACCINATION COMPRISING NUCLEIC  
ACID AND/OR POLYPEPTIDE  
SEQUENCES OF CHLAMYDIA

Group Art Unit: 1635

Examiner: FORD, VANESSA L.

Atty. Dkt. No.: UTSD:736US/MBW

**DECLARATION OF AKIRA TAKASHIMA, M.D., PH.D.**

I, Akira Takashima, M.D., Ph.D., hereby declare as follows:

1. I am a Professor at the University of Texas Southwestern Medical Center. I have extensive experience in the fields of immunology and molecular biology. References containing examples of my work are included in my *Curriculum Vitae*. A copy of my *Curriculum Vitae* is attached as Exhibit 1.

2. I have reviewed relevant documents relating to the above-referenced patent application. Specifically, I have reviewed the Office Action dated November 10, 2004, the specification of

the application, the pending claims, and the amended claims. In light of these documents, and my knowledge of immunology and molecular biology, I make the following statements.

3. I understand that the claims in this application relate to methods of immunizing an animal comprising providing to the animal at least one *Chlamydia psittaci* antigen in an amount effective to induce an immune response against *Chlamydia psittaci*.

4. I also understand that the Examiner has rejected several claims of the application on the grounds that the specification is not enabling for all antigenic fragments of SEQ ID NOs: 7, 9, 11, and 13 encompassed by the claims. I do not find this to be the case.

5. Based on my experience and knowledge in the fields of immunology and molecular biology, I believe that a scientist of standard skill in immunology or molecular biology would be capable of eliciting an immune response in an animal against *Chlamydia psittaci* using a number of antigenic fragments of SEQ ID NOs: 7, 9, 11, and 13 by following the teachings in the specification.

6. The present specification describes an “antigenic fragment” as a fragment that can elicit an immune response in an animal (p. 13, ln. 19-20). The specification provides further description of “fragments” of the SEQ ID NOs: 7, 9, 11, and 13 at page 13, lines 9-18. Based on these descriptions, a person of standard skill in molecular biology or immunology would understand an antigenic fragment of SEQ ID NOs: 7, 9, 11, or 13 to refer to a fragment of at least 5 contiguous amino acids of SEQ ID NOs: 7, 9, 11, or 13, but fewer than the full length of SEQ ID NOs: 7, 9, 11, or 13, capable of eliciting an immune response in an animal.

7. I have reviewed the data presented in Examples 1 through 12 of the present specification. These data show, among other things, that the 443 amino acid polypeptide of SEQ ID NO: 9 can be used to immunize an animal (*see e.g.*, p. 75, Table 3; p. 80, ln. 2-6). Furthermore, these data show that a 149 amino acid fragment (SEQ ID NO: 7) of SEQ ID NO: 9 can also be used to immunize an animal (*see e.g.*, p. 75, Table 3; p. 80, ln. 2-6). Based on these results, a scientist will understand that there would likely be other antigenic fragments of SEQ ID NO: 9 and SEQ ID NO: 7 that would elicit an immune response in an animal.

8. The data in the present specification also show that the 100 amino acid polypeptide of SEQ ID NO: 13 can be used to immunize an animal (*see e.g.*, p. 75, Table 3; p. 80, ln. 2-6). In addition, a 41 amino acid fragment (SEQ ID NO: 11) of SEQ ID NO: 13 can also be used to immunize an animal (*see e.g.*, p. 75, Table 3; p. 80, ln. 2-6). Based on these results, a scientist will understand that there would likely be other antigenic fragments of SEQ ID NO: 11 and SEQ ID NO: 13 that would elicit an immune response in an animal.

9. The present specification provides guidance for making and evaluating antigenic fragments of SEQ ID NOs: 7, 9, 13, and 11. First, the specification provides the nucleic acid and amino acid sequences of these antigens as a starting point from which a scientist could make other antigenic fragments. As described in the specification, it is also known that certain amino acids may be substituted for other amino acids in a protein structure without appreciable loss of interactive binding capacity with antigen-binding regions of antibodies (p. 26, ln. 18-20).

10. Furthermore, it is also known to scientists in the fields of molecular biology and immunology that immunogenic proteins typically contain multiple immunogenic epitopes or determinants. A scientist of standard skill would be capable of identifying antigenic fragments of

SEQ ID NOs: 7, 9, 11, and 13 by following the teachings in the specification. For example, as described in the present specification at page 25, lines 8-20, antigenic determinants of a polypeptide may be identified by preparing a range of cDNAs encoding peptides lacking successively longer fragments of the C-terminus of the polypeptide. The immunogenic activity of each of these peptides then identifies those fragments or domains of the polypeptide that are essential for antigenic activity. Further experiments in which only a small number of amino acids are removed or added at each iteration then allows the location of other antigenic determinants of the polypeptide. Scanning a full-length antigenic polypeptide for antigenic epitopes or determinants is routine in the field of immunology. Thus, a scientist of standard skill in molecular biology or immunology could identify antigenic fragments of SEQ ID NOs: 7, 9, 11, and 13 using only routine screening techniques as described in the present specification.

11. In conclusion, a molecular biologist or immunologist could practice the presently claimed invention using antigenic fragments of SEQ ID NOs: 7, 9, 11, or 13 by following the teachings of the present specification.

12. I declare that all statements made of my knowledge are true and all statements made on the information are believed to be true; and, further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issued thereupon.

Date:

2-23-05

A handwritten signature in black ink, appearing to read 'Akira Takashima', written over a horizontal line.

Akira Takashima, M.D., Ph.D.

**CURRICULUM VITAE**  
**Akira Takashima, M.D., Ph.D.**

**Date of Birth:** February 24, 1954

**Place of Birth:** Gifu, Japan

**Marital Status:** Married, 1 child

**Nationality:** Japanese

**Visa Status:** Permanent Resident

**Present address:** UT Southwestern Medical Center  
Department of Dermatology  
5323 Harry Hines Boulevard  
Dallas, Texas 75390-9069

**Degrees:** M.D. Nagoya City University, 1981  
Ph.D. Nagoya City University, 1989

**Education:** 1975 - 1981 Nagoya City University Medical School, Nagoya, Japan

**Research and Professional Experience:**

1981-1982	Resident, Department of Dermatology, Nagoya City University Medical School Nagoya, Japan
1982-1983	Faculty ("joshu"), Department of Dermatology, Nagoya City University
1983-1985	Research Fellow, Department of Cell Biology, UT Southwestern Medical Center
1985-1986	Research Fellow, Department of Dermatology, UT Southwestern Medical Center
1986-1991	Faculty ("joshu"), Department of Dermatology, Nagoya City University
1990-1992	Visiting Assistant Professor of Dermatology, UT Southwestern Medical Center
1992-1994	Assistant Professor of Dermatology, UT Southwestern Medical Center
1994-1996	Associate Professor of Dermatology, UT Southwestern Medical Center
1997-Present	Professor of Dermatology, UT Southwestern Medical Center
1997-Present	Director of Cutaneous Biology Laboratory, UT Southwestern Medical Center
1998-Present	Vice Chairman for Research, Dermatology, UT Southwestern Medical Center
1999-2001	Director for Immunodermatopathology Fellowship Training, Dermatology UT Southwestern Medical Center
1999-Present	Thomas L. Shields, M.D. Professorship, UT Southwestern Medical Center
1992-Present	Faculty of Immunology Program, Graduate School of Biomedical Sciences

UT Southwestern Medical Center

1999-Present Faculty of Molecular Microbiology Program, Graduate School of Biomedical Sciences  
UT Southwestern Medical Center

2002-Present Professor of Internal Medicine, Center for Biomedical Inventions  
UT Southwestern Medical Center

**Membership in Academic Societies:** American Society for Clinical Investigation  
American Association for Cancer Research  
American Association of Immunologists  
American Federation of Clinical Research  
American Society for Photobiology  
Society for Investigative Dermatology  
Molecular Medicine Society  
Japanese Society for Investigative Dermatology  
Japanese Dermatological Association  
New York Academy of Sciences

**Awards and Honors:** CE.R.I.E.S. Award (1996)  
American Society for Clinical Investigation (1998)  
William Montagna Lectureship (2004)

**Editorial Responsibilities:**

1997-2001 Associate Editor, *Journal of Immunology*  
2001 Volume Editor, *Chemical Immunology*, Vol 79:  $\gamma\delta$  T cells  
2000-present International Advisory Board, *Journal of Dermatology*  
2001-present Section Editor, *Journal of Immunology*  
2002-present Associate Editor, *Journal of Investigative Dermatology*  
2002-present Regional Editor, *Journal of Dermatological Science*

**Scientific Activities:**

1997-2000 Medical and Scientific Committee, Dermatology Foundation  
2002-2003 Scientific Advisory Board, National Alopecia Areata Foundation  
2001-present Scientific Program Committee, Society of Investigative Dermatology

**Patents:**

1. Unique Dendritic Cell-Associated C-Type Lectins, Dectin-1 and Dectin-2; Compositions and Uses Thereof:  
A Takashima, Ariizumi K. US Patent Number 6046158, 4/4/00
2. Modulators of Polysaccharides and Uses Thereof: US Patent Number 6,653,285, 11/25/03  
A Takashima, ME Mummert, M Mohamadzadeh
3. Hybrid Dendritic Cells to Induce Antigen-specific Modulation of the Immune System:  
H Matsue, A Takashima US Patent Application Serial No. 09/536,176
4. Transcription Factor Inhibitors to Prevent and/or Treat Radiation-Induced Skin Changes:  
K Abeyama, PR Bergstresser, A Takashima US Patent Application Serial No. 09/534,837



5. Inhibitors of Glycosaminoglycans  
M Mummert, **A Takashima** US Patent Application Serial No. 09/532,709
6. Diagnosis and Treatment of Inflammation  
T Kumamoto, N Mizumoto, **A Takashima** Provisional Patent Application filed March 1, 2001
7. *In Situ* Langerhans Cell Vaccine  
**A Takashima**, T Kumamoto US Patent Application Serial No. 09/808,555
8. Ebselen as a Therapeutic for Preventing Diseases Associated with Dendritic Cell  
**A Takashima** Provisional Patent Application filed March 28, 2003

## BIBLIOGRAPHY

### Original Articles

1. Takashima A, Yoshikawa K: Contact allergy to isothipendyl. *Contact Dermatitis* 9:429-430, 1983.
2. Takashima A, Grinnell F: Human keratinocyte adhesion and phagocytosis prompted by fibronectin. *J Invest Dermatol* 83:352-358, 1984.
3. Takashima A, Grinnell F: Fibronectin-mediated keratinocyte migration and initiation of fibronectin receptor function in vitro. *J Invest Dermatol* 85:304-308, 1985.
4. Takashima A, Billingham RE, Grinnell F: Activation of rabbit keratinocyte fibronectin receptor function in vivo during wound healing. *J Invest Dermatol* 86:585-590, 1986.
5. Grinnell F, Takashima A, Lamke-Seymour: Differentiation of keratinocytes on fibroblast reorganized collagen gels. *Cell Tissue Res* 246:13-21, 1986.
6. Kuziel WA, Takashima A, Bonyhadi M, Bergstresser PR, Allison JP, Tigelaar RE, Tucker PW: Regulation of T-cell receptor  $\gamma$ -chain RNA expression in murine Thy-1<sup>+</sup> dendritic epidermal cells. *Nature* 328:263-266, 1987.
7. Takashima A, Nixon-Fulton JL, Bergstresser PR, Tigelaar RE: Thy-1<sup>+</sup> dendritic epidermal cells in mice: Precursor frequency analysis and cloning of Concanavalin A-reactive cells. *J Invest Dermatol* 90:671-678, 1988.
8. Takashima A, Sunohara A, Mizuno N: Comparison of the relative therapeutic efficacy of 7-methyl pyridopsoralen and 8-methoxypsoralen in photochemotherapy in psoriasis treatment. *J Dermatol* 15:195-201, 1988.
9. Takashima A, Sunohara A, Matsunami E, Mizuno N: Comparison of therapeutic efficacy of topical PUVA, oral etretinate, and combined PUVA and etretinate for the treatment of psoriasis and development of PUVA lentiginos and antinuclear antibodies. *J Dermatol* 15:473-479, 1988.
10. Ichikawa K, Takashima A, Yasuda S, Mizuno N: UVB enhances tissue plasmin activity of rabbit skin and UVB induces plasminogen activator production by PAM 212 cells. *Photomed Photobiol* 10:181-184, 1988.
11. Takashima A, Yasuda S, Mizuno N: Development of phototherapy for acute carbon monoxide intoxication. *Suzuken Memorial Foundation* 108-113, 1988 (in Japanese).
12. Takashima A, Matsunami E, Yamamoto K, Mizuno N: Topical PUVA therapy using a whole body UVA irradiating unit, Dermalay M-DMR-TS. *Nishinihon Hifuka* 51:329-334, 1989 (in Japanese).
13. Takashima A: Effect of UV irradiation on plasminogen activator production by PAM 212 cells. *Nagoya City University Medical Journal*. 40:173-179, 1989 (in Japanese).
14. Takashima A, Ichikawa K, Yasuda S, Mizuno N: Induction of plasminogen activator by UV light in mouse keratinocyte-derived cell line, PAM 212. *Dermatologica* 179 (suppl 1): 133, 1989.
15. Ichikawa K, Takashima A, Yasuda S, Mizuno N: Enhanced rabbit skin plasmin activity by UV irradiation. *Dermatologica* 179 (suppl 1): 132, 1989.
16. Takashima A, Yamamoto K, Mizuno N: Photochemotherapy using 4,6,4'-trimethylangelicin in psoriasis treatment. *Photomed Photobiol* 11:155-162, 1989.

17. Matsunami E, **Takashima A**, Mizuno N, Jinno T, Ito H: Topical PUVA, etretinate and combined PUVA and etretinate for palmoplantar pustulosis: Comparison of therapeutic efficacy and influence of tonsillar and dental focal infection. *J Dermatol* 17:92-96, 1990.
18. Okubo I, Niwa M, **Takashima A**, Nishikami N, Gasa S, Sasaki S: Human seminal plasma Zn- $\alpha_2$ -glycoprotein: Its purification and properties as compared with human plasma Zn- $\alpha_2$ -glycoprotein. *Biochem Biophys Acta* 1034:152-156, 1990.
19. Koji M, Kanzaki T, **Takashima A**: Polyprenoic acid, E-5166, is effective in inhibiting the proliferation of keratinocytes in vitro. *Arch Dermatol Res* 282:135-138, 1990.
20. **Takashima A**, Morita A, Tsuji T: Treatment of PUVA- and retinoid-PUVA-resistant severe psoriasis with systemic cyclosporin A. *J Dermatol* 17:482-488, 1990.
21. Morita A, **Takashima A**, Nagai M, Dall'Acqua F: Treatment of mycosis fungoides and parapsoriasis en plaque with topical PUVA using a monofunctional furocoumarin derivative 4,6,4'-trimethylangelicin. *J Dermatol* 17:545-549, 1990.
22. **Takashima A**, Matsunami E, Yamamoto K, Kitajima S, Mizuno N: Cutaneous carcinoma and PUVA lentigines in Japanese patients with psoriasis treated with topical PUVA: A follow-up study of 214 patients. *Photoderm Photoimmun Photomed* 7:218-221, 1991.
23. **Takashima A**, Morita A: Genomic, phenotypic and functional analyses of T cells in patients with psoriasis undergoing systemic cyclosporin A treatment. *J Invest Dermatol* 96:376-382, 1991.
24. **Takashima A**, Yamamoto K, Kimura S, Takakuwa Y, Mizuno N: Allergic contact and photocontact dermatitis due to psoralens in patients with psoriasis treated with topical PUVA. *Br J Dermatol* 124:37-42, 1991.
25. **Takashima A**, Yasuda S, Mizuno N: Determination of the action spectrum for UV-induced plasminogen activator synthesis in mouse keratinocytes in vitro. *J Dermatol Sci* 4:11-17, 1992.
26. Matsue H, Rothberg KG, **Takashima A**, Kamen BA, Anderson RGW, Lacey SW: Folate receptor allows cells to grow in low concentrations of 5-methyltetrahydrofolate. *Proc Natl Acad Sci USA* 89:6006-6009, 1992.
27. Matsue H, Cruz PD Jr., Bergstresser PR, **Takashima A**: Langerhans cells are the major source of mRNA for IL-1 $\beta$  and MIP-1 $\alpha$  among unstimulated mouse epidermal cells. *J Invest Dermatol* 99:537-431, 1992.
28. Kanazaki T, Morita A, **Takashima A**: Follicular keratosis of the chin. *J Amer Acad Dermatol* 26:134-135, 1992.
29. Kaminski MJ, Bergstresser PR, **Takashima A**: In vivo activation of mouse dendritic epidermal T cells in sites of contact dermatitis. *Eur J Immunol* 23:1715-1718, 1993.
30. Matsue H, Cruz PD Jr., Bergstresser PR, **Takashima A**: Profiles of cytokine mRNA expressed by dendritic epidermal T cells in mice. *J Invest Dermatol* 101:537-542, 1993.
31. Matsue H, Bergstresser PR, **Takashima A**: Reciprocal cytokine-mediated cellular interactions in mouse epidermis: promotion of  $\gamma\delta$  T cell growth by IL-7 and TNF $\alpha$  and inhibition of keratinocyte growth by  $\gamma$ IFN. *J Invest Dermatol* 101:543-548, 1993. .

32. Chung BS, Bergstresser PR, **Takashima A**: Mouse dendritic epidermal T cells exhibit chemotactic migration toward Pam 212 keratinocyte culture supernatants. *J Invest Dermatol* 101:371-376, 1993.
33. Kaminski MJ, Cruz PD Jr., Bergstresser PR, **Takashima A**: Killing of skin-derived tumor cells by mouse dendritic epidermal T cells. *Cancer Res* 53:4014-4019, 1993.
34. Mathew PA, Garni-Wagner BA, Land K, **Takashima A**, Stoneman E, Bennet M, Kumar V. Cloning and characterization of a molecule associated with non-MHC restricted killing mediated by natural killer cells and T cells. *J Immunol* 151:5328-5337, 1993.
35. Matsue H, Bergstresser PR, **Takashima A**: Keratinocyte-derived IL-7 serves as a growth factor for dendritic epidermal T cells in mouse skin. *J Immunol* 151:6012-6019, 1993.
36. Fehr B, **Takashima A**, Matsue H, Gerometta J, Bergstresser P, Cruz, P.D., Jr.: Contact sensitization induces proliferation of heterogeneous populations of hapten-specific T cells. *Exp Dermatol* 3:189-197, 1994.
37. Lyson K, Ceriani G, **Takashima A**, Catania A, Lipton JM: Binding of anti-inflammatory  $\alpha$ -melanocyte-stimulating-hormone peptides and proinflammatory cytokines to receptors on melanoma cells. *Neuroimmunomodulation* 1:121-126, 1994.
38. Xu S, Ariizumi K, Caceres-Dittmar G, Edelbaum D, Hashimoto K, Bergstresser PR, **Takashima A**: Successive generation of antigen-presenting, dendritic cell lines from murine epidermis. *J Immunol* 154:2697-2705, 1995.
39. Pandya AG, Sontheimer RD, Cockerell CJ, **Takashima A**, Piepkorn M: Papulonodular mucinosis associated with systemic lupus erythematosus: Possible mechanisms of increased glycosaminoglycan accumulation. *J Amer Acad Dermatol* 32:199-205, 1995.
40. Ariizumi K, Meng Y, Bergstresser PR, **Takashima A**: IFN- $\gamma$ -dependent IL-7 gene regulation in keratinocytes. *J Immunol* 154:6931-6039, 1995.
41. Caceres-Dittmar G, Ariizumi K, Xu S, Tapia FJ, Bergstresser PR, **Takashima A**: Hydrogen peroxide mediates UV-induced impairment of antigen presentation in a murine epidermal-derived dendritic cell line. *Photochem Photobiol* 62:176-183, 1995.
42. Schuhmachers G, Ariizumi K, Mathew PA, Bennett M, Kumar V, **Takashima A**: Activation of murine epidermal  $\gamma\delta$  T cells through surface 2B4. *Eur J Immunol* 25:1117-1120, 1995.
43. **Takashima A**, Edelbaum D, Kitajima T, Shaddock RK, Gilmore G, Xu S, Taylor RS, Bergstresser PR, Ariizumi K: Colony-stimulating factor-1 secreted by fibroblasts promotes the growth of dendritic cell lines (XS series) derived from murine epidermis. *J Immunol* 154:5128-5135, 1995.
44. Xu S, Ariizumi K, Edelbaum D, Bergstresser PR, **Takashima A**: Cytokine-dependent regulation of growth and maturation in murine epidermal dendritic cell lines. *Eur J Immunol* 25:1018-1024, 1995.
45. Asahina A, Moro O, Hosoi J, Lerner EA, Xu S, **Takashima A**, Granstein RD: Specific induction of cAMP in Langerhans cells by calcitonin gene-related peptide: Relevance to functional effects. *Proc Natl Acad Sci USA* 92:8323-8327, 1995.
46. Schuhmachers G, Xu S, Bergstresser PR, **Takashima A**: Identity and functional properties of novel skin-derived fibroblast lines (NS series) that support the growth of epidermal-derived dendritic cell lines. *J Invest Dermatol* 105:225-230, 1995.

47. Ariizumi K, Kitajima T, Bergstresser PR, **Takashima A**: Interleukin-1 $\beta$  converting enzyme in murine Langerhans cells and epidermal-derived dendritic cell lines. *Eur J Immunol* 25:2137-2140, 1995.
48. Schuhmachers G, Ariizumi K, Mathew PA, Bennett M, Kumar V, **Takashima A**: 2B4, a new member of the immunoglobulin gene superfamily, is expressed on murine dendritic epidermal T cells and plays a functional role in their killing of skin tumors. *J Invest Dermatol* 105:592-596, 1995.
49. Edelbaum D, Mohamadzadeh M, Bergstresser PR, Sugamura K, **Takashima A**: Interleukin (IL)-15 promotes the growth of murine epidermal  $\gamma\delta$  T cells by a mechanism involving the  $\beta$ - and  $\gamma_c$ -chains of the IL-2 receptor. *J Invest Dermatol* 105:837-843, 1995.
50. Xu S, Bergstresser PR, **Takashima A**: Phenotypic and functional heterogeneity among murine epidermal-derived dendritic cell clones. *J Invest Dermatol* 105:831-836, 1995.
51. Kitajima T, Ariizumi K, Bergstresser PR, **Takashima A**: T cell-dependent loss of proliferative responsiveness to CSF-1 by a murine epidermal-derived dendritic cell line, XS52. *J Immunol* 155:5190-5197, 1995.
52. Kitajima T, Ariizumi K, Mohamadzadeh M, Edelbaum D, Bergstresser PR, **Takashima A**: T cell-dependent secretion of IL-1 $\beta$  by a dendritic cell line (XS52) derived from murine epidermis. *J Immunol* 155:3794-3800, 1995.
53. Mohamadzadeh M, **Takashima A**, Dougherty I, Knop J, Bergstresser PR, Cruz PD Jr.: Ultraviolet B radiation up-regulates the expression of IL-15 in human skin. *J Immunol* 155:4492-4496, 1995.
54. Mohamadzadeh M, Ariizumi K, Sugamura K, Bergstresser PR, **Takashima A**: Expression of the common cytokine receptor  $\gamma$  chain by murine dendritic cells including epidermal Langerhans cells. *Eur J Immunol* 26:156-160, 1996.
55. Ono M, Ariizumi K, Bergstresser PR, **Takashima A**: IL-7 upregulates T cell receptor/CD3 expression by cultured dendritic epidermal T cells. *J Dermatol Sci* 11:89-96, 1996.
56. Ariizumi K, Bergstresser P, **Takashima A**: Wavelength-specific induction of immediate early genes by ultraviolet radiation. *J Dermatol Sci* 12:147-155, 1996.
57. Schuhmachers G, Ariizumi K, Kitajima T, Edelbaum D, Xu S, Shadduck RK, Gilmore GL, Taylor RS, Bergstresser PR, **Takashima A**: UVB radiation interrupts cytokine-mediated support of an epidermal-derived dendritic cell line (XS52) by a dual mechanism. *J Invest Dermatol* 106:1023-1029, 1996.
58. Mohamadzadeh M, Poltorak AN, Bergstresser PR, Beutler B, **Takashima A**: Dendritic cells produce macrophage inflammatory protein-1 $\gamma$ , a new member of the CC chemokine family. *J Immunol* 156:3102-3106, 1996.
59. Mohamadzadeh M, McGuire MJ, Smith DJ, Gaspari AA, Bergstresser PR, **Takashima A**: Functional roles for granzymes in murine epidermal  $\gamma\delta$  T cell-mediated killing of tumor targets. *J Invest Dermatol* 107:738-742, 1996.
60. Qureshi AA, Hosoi J, Xu S, **Takashima A**, Granstein R, Lerner EA: Langerhans cells express inducible nitric oxide synthase and produce nitric oxide. *J Invest Dermatol* 107:815-821, 1996.
61. Kitajima T, Ariizumi K, Bergstresser PR, **Takashima A**: A novel mechanism of glucocorticoid-induced immune suppression: The inhibition of T cell-mediated terminal maturation of a murine dendritic cell line. *J Clin Invest* 98:142-147, 1996.

62. Yokota K, Ariizumi K, Kitajima T, Bergstresser PR, Street NE, **Takashima A**: Cytokine-mediated communication between dendritic epidermal T cells and Langerhans cells: *In vitro* studies using cell lines. *J Immunol* 157:1529-1537, 1996.
63. Kitajima T, Caceres-Dittmar G, Tapia FJ, Jester J, Bergstresser PR, **Takashima A**: T cell-mediated terminal maturation of dendritic cells: Loss of adhesive and phagocytotic capacities. *J Immunol* 157:2340-2347, 1996.
64. Kitajima T, Ariizumi K, Bergstresser PR, **Takashima A**: UVB radiation sensitizes an epidermal dendritic cell line (XS52) to undergo apoptosis in response to antigen-specific interaction with T cells. *J Immunol* 157:3312-3316, 1996.
65. Catalina M.D., Carroll MC, Arizpe H, **Takashima A**, Estess P, Siegelman MH: The route of antigen entry determines the requirement for L-selectin during immune responses. *J Exp Med* 184:2341-2351, 1996.
66. Ogoshi M, **Takashima A**, Taylor RS: Mechanisms regulating telomerase activity in murine T cells. *J Immunol* 158:622-628, 1997.
67. Torii H, Hosoi J, Beissert S, Xu S, Fox FE, Asahina A, Takashima A, Rook AH, Granstein RD: Regulation of cytokine expression in macrophages and the Langerhans cell-like line XS52 by calictonin gene-related peptide. *J Leukocyte Biol* 61:216-223, 1997.
68. Aragane Y, Schwarz A, Luger TA, Ariizumi K, **Takashima A**, Schwarz T: Ultraviolet light suppresses IFN $\gamma$ -induced IL-7 gene transcription in murine keratinocytes by interfering with interferon regulatory factors. *J Immunol* 158:5393-5399, 1997.
69. Timares L, **Takashima A**, Johnston SA: Quantitative analysis of the immunopotency of genetically transfected dendritic cells. *Proc Natl Acad Sci USA* 95:13147-13152, 1998.
70. Hosoi J, Tsuchiya T, Denda M, Ashida Y, **Takashima A**, Granstein RD, Koyama J: Modification of LC phenotype and suppression of contact hypersensitivity response by stress. *J Cutan Med Surg* 3:79-84, 1998.
71. Matsue H, Edelbaum D, Hartmann AC, Morita A, Bergstresser PR, Yagita H, Okumura K, and **Takashima A**: Dendritic cells undergo rapid apoptosis *in vitro* during antigen-specific interaction with CD4<sup>+</sup> T cells. *J Immunol* 162:5287-5298, 1999.
72. Matsue H, Matsue K, Walters M, Okumura K, Yagita H, and **Takashima A**: Induction of antigen-specific immunosuppression by CD95L cDNA-transfected "killer" dendritic cells. *Nature Med* 5:930-937, 1999.
73. Ariizumi K, Shen G-L, Shikano S, Xu S, Ritter III R, Kumamoto T, Edelbaum D, Morita A, Bergstresser PR, **Takashima A**: Identification of a novel, dendritic cell-associated molecule, dectin-1, by subtractive cDNA cloning. *J Biol Chem* 275: 20157-20167, 2000.
74. Ariizumi K, Shen G-L, Shikano S, Ritter III R, Zukas P, Edelbaum D, Morita A, **Takashima A**: Cloning of a second dendritic cell-associated c-type lectin (dectin-2) and its alternatively spliced isoforms. *J Biol Chem* 275:11957-11963, 2000.
75. Hayashi S, Johnston SA, **Takashima A**: Induction of Th2-directed immune responses by IL-4-transduced dendritic cells in mice. *Vaccine* 18:3097-3105, 2000.
76. Abeyama K, Eng W, Jester JV, Edelbaum D, Cockerell CJ, Bergstresser PR, **Takashima A**: A role for NF $\kappa$ B gene transactivation in sunburn. *J Clin Invest* 105:1751-1759, 2000.

77. Mummert ME, Mohamadzadeh M, Mummert DI, Mizumoto N, **Takashima A**: Development of a peptide inhibitor of hyaluronan-mediated leukocyte trafficking. *J Exp Med* 192:769-779, 2000.
78. Fehr BS, **Takashima A**, Bergstresser PR, Cruz PD Jr: T cells reactive to keratinocyte antigens are generated during induction of contact hypersensitivity in mice. A model for autoeczematization in humans? *Am J Contact Derm* 11:145-154, 2000
79. Bouis DA, Popova TG, **Takashima A**, Norgard MV: Dendritic cells phagocytose and are activated by treponema pallidum. *Infect Immunol* 69:518-28, 2001.
80. Morita A, Ariizumi K, Ritter R, Jester JV, Kumamoto T, Johnston SA, **Takashima A**: Development of Langerhans cells-targeted gene expression system using dectin-2 promoter. *Gene Therapy* 8:1729-1737, 2001.
81. Matsue H, Matsue K, Kusuhaara M, Kumamoto T, Okumura K, Yagita H, **Takashima A**: Immunosuppressive properties of CD95L-transduced "killer" hybrids created by fusing donor- and recipient-derived dendritic cells. *Blood* 98:3465-3472, 2001.
82. Yokota K, **Takashima A**, Bergstresser PR, Ariizumi K: Identification of a human homologue of the dendritic cell-associated C-type lectin-1, dectin 1. *Gene* 272:51-60, 2001.
83. Kumamoto T, Huang EK, Paek HJ, Morita A, Matsue H, Valentini RF, **Takashima A**: Induction of tumor-specific protective immunity by *in situ* Langerhans cell vaccine *Nature Biotech* 20:64-69, 2002.
84. Mizumoto N, Kumamoto T, Robson SC, Sevigny J, Matsue H, Enjyoji K, **Takashima A**: CD39 is the dominant Langerhans cell-associated ecto-NTPDase: modulatory roles in inflammation and immune responsiveness. *Nature Med* 8:358-365, 2002.
85. Kusuhaara M, Matsue K, Edelbaum D, Loftus J, **Takashima A**, Matsue H: Killing of naïve T cells by CD95L-transfected dendritic cells (DC): *In vivo* study using killer DC-DC hybrids and CD4<sup>+</sup> T cells from DO11.10 mice. *Eur J Immunol* 32:1035-1043, 2002.
86. Mummert M, Mummert D, Edelbaum D, Hui F, Matsue H, **Takashima A**: Synthesis and surface expression of hyaluronan by dendritic cells and its potential role in antigen presentations. *J Immunol* 169:4322-4331, 2002
87. Matsue H, Yang C, Matsue K., Edelbaum D, Mummert, M, **Takashima A**: Contrasting impacts of immunosuppressive agents (rapamycin, FK506, cyclosporin A, and dexamethasone) on bi-directional dendritic cell-T cell interaction during antigen presentation. *J Immunol* 169:3555-3564, 2002.
88. Wolfe T, Asseman C, Hughes A, Matsue H, **Takashima A**, von Herrath MG: Elimination of anti-viral CD8 lymphocytes *in vivo* with killer dendritic cells expressing FAS-L – reduction of viral immunopathology while maintaining clearance. *J Immunol* 169:4867-4782, 2002.
89. Mummert ME, Mummert DI, Ellinger L, **Takashima A**: Functional roles of hyaluronan in B16-F10 melanoma growth and experimental metastasis in mice. *Mol Cancer Therapeutics* 2:295-300, 2003.
90. Lu M, Zhang M, Kitchens RL, Fosmire S, **Takashima A**, Munford RS: Stimulus-dependent deacylation of bacterial lipopolysaccharide by dendritic cells. *J Exp Med* 197:1745-1754, 2003.
91. Kumamoto T, Shalhevet D, Matsue H, Mummert ME, Ward BR, Jester JV, **Takashima A**: Hair follicles serve as local reservoirs of skin mast cell precursors. *Blood* 103:1654-1660, 2003.
92. Timares L, Safer KM, Qu B, **Takashima A**, Johnston SA: Drug-inducible dendritic cell-based genetic immunization. *J Immunol* 170:5483-5490, 2003.

93. Mizumoto N, Mummert ME, Shalhevet D, **Takashima A**: Keratinocyte ATP release assay for testing skin irritating potentials of structurally diverse chemicals. *J Invest Dermatol* 121:1066-1072, 2003.
94. Mummert DI, **Takashima A**, Ellinger L, Mummert MA: Involvement of hyaluronan in epidermal Langerhans cell maturation and migration *in vivo*. *J Dermatol Sci* 33:91-97, 2003.
95. Matsue H, Edelbaum, Shalhevet D, Mizumoto N, Yang C, Mummert ME, Oeda J, Masayasu H, **Takashima A**: Generation and function of reactive oxygen species in dendritic cells during Ag presentation. *J Immunol* 171:3010-3018, 2003.
96. Mummert DI, **Takashima A**, Mummert ME: Langerhans cells in CD44-deficient mice emigrate from the epidermis but fail to reach the lymph nodes after hapten application. *J Invest Dermatol* 122:846-847, 2004.
97. Gao J, **Takashima A**: Cloning and characterization of *Trichophyton rubrum* genes encoding actin, Tri r2, and Tri r4. *J Clin Microbiol* 42:3298-3299, 2004.
98. McGuire M, Sykes K, Samli K, Timares L, Barry M, Stemke-Hale K, Tagliaferri F, Logan M, Jansa K, **Takashima A**, Brown K, Johnston SA: A library-selected, Langerhans cell-targeting peptide enhances an immune response. *DNA & Cell Biology* 23:742-752, 2004.
99. Matsue H, Matsue K, Edelbaum, Walters M, Morita A, **Takashima A**. New strategy for efficient selection of dendritic cell-tumor hybrids and clonal heterogeneity of resulting hybrids. *Cancer Biol & Therapy* 3:1145-1151, 2004
100. Huebeschman ML, Hunt J, Munjuluri B, **Takashima A**, Garner HR. Design and performance of variable spectrum synthesizer. *Rev Sci Instruments* 75:4845-4855, 2004.
101. Mizumoto N, Hui F, Edelbaum D, Weil MR, Wren JD, Shalhevet D, Matsue H, Liu L, Garner HR, **Takashima A**: Differential activation profiles of multiple transcription factors during dendritic cell maturation. *J Invest Dermatol* (in press) 2005.

#### **Review Articles and Chapters.**

1. **Takashima A**, Yaoita H: Anti-basement zone antibodies. *Hifukano Rinsho* 28:1189-1201, 1986 (in Japanese).
2. Grinnell F, Toda K-I, **Takashima A**: Activation of keratinocyte fibronectin receptor function during cutaneous wound healing. *J Cell Sci. Suppl* 8:199-209, 1987.
3. Grinnell F, Toda K-I, **Takashima A**: Role of fibronectin in epithelialization and wound healing. Growth Factors and Other Aspects of Wound Healing: Biological and Clinical Implications, pp 259-272, 1988, Alan R. Liss.
4. Tigelaar R, Nixon-Fulton J, **Takashima A**, Kuziel W, Takijiri C, Lewis J, Tucker P, Bergstresser P: Effect of keratinocyte cytokines on Thy-1<sup>+</sup> dendritic epidermal cells. Endocrine, Metabolic and Immunologic Functions of Keratinocytes. *Annals of New York Academy of Science*, 548:271-282, 1988.
5. **Takashima A**: Topical PUVA, etretinate and Re-PUVA in psoriasis treatment. *Symposium on Psoriasis* 1988, pp 76-79, 1989 (in Japanese).



6. **Takashima A**, Matsunami E, Sunohara A, Yamamoto K, Mizuno N: Topical PUVA: therapeutic efficacy and side effects. *Jpn J Dermatol* 99:1405-1406, 1989 (in Japanese).
7. **Takashima A**: Carcinogenesis of PUVA. *Gendai Hifukagaku Taikei* 90A:111-113, 1990 (in Japanese).
8. **Takashima A**, Yamamoto K, Mizuno N: Allergic photocontact dermatitis to furocoumarin. *Hifubyo Shinryo* 12:433-436, 1990 (in Japanese).
9. **Takashima A**, Matsunami E, Mizuno N: Combined PUVA and retinoid in the treatment of psoriasis and palmoplantar pustulosis. *Rinsho Hifuka* 44, (in Japanese), 1991.
10. **Takashima A**, Mizuno N: PUVA therapy: Indication and methods. *Hifubyo Taikei*, (in Japanese) 1991.
11. **Takashima A**: PUVA Therapy. In, Photosensitivity, Ed. by A. Sato, Kanehara Press, Tokyo, (in Japanese) 1992.
12. Matsue H, Cruz PD Jr, Bergstresser PR, **Takashima A**: Cytokine expression by epidermal cell subpopulations. *J Invest Dermatol* 99:42S-45S, 1992.
13. Bergstresser PR, Cruz PD Jr, Niederkorn JY, **Takashima A**: Third International Workshop on Langerhans Cells: Discussion Overview. *J Invest Dermatol* 99:1S-4S, 1992.
14. Bergstresser PR, Cruz PD Jr., **Takashima A**: Dendritic epidermal T cells: Lessons from mice for humans. *J Invest Dermatol* 100:80S-83S, 1993.
15. Bergstresser PR, Cruz PD Jr., Ariizumi K, **Takashima A**: Ultraviolet Radiation-Induced Immune Suppression. In, Biologic Effects of Light 1993, Proceedings of a Symposium. Ed. G. Jung, M.F. Holick, Walter de Gruyter, New York, 1994, pp 571-584.
16. **Takashima A**, Xu S, Ariizumi K, Bergstresser PR: Establishment and characterization of antigen-presenting cell lines (XS series) derived from newborn mouse epidermis. In Dendritic Cells in Fundamental and Clinical Immunology, Eds. J Banchereau and D Schmitt, Plenum Publishing Company Ltd., London, pp 159-162, 1995.
17. **Takashima A**: UVB-dependent modulation of epidermal cytokine network: Roles in UVB-induced depletion of Langerhans cells and dendritic epidermal T cells. *J Dermatol* 22:876-887, 1995.
18. Bergstresser PR, **Takashima A**: Ultraviolet Radiation-Mediated Defects in Langerhans Cell Function, in The Immune Functions of Epidermal Langerhans Cells, Ed. Heidrun Moll, R.G. Landes Company, Springer-Verlag, London, pp 119-140, 1995.
19. **Takashima A**, Matsue H, Bergstresser PR, Ariizumi K: Interleukin-7-dependent interaction of dendritic epidermal T cells with keratinocytes. *J Invest Dermatol* 105:50S-53S, 1995.
20. **Takashima A** and Bergstresser PR: Impact of UVB Radiation on the Epidermal Cytokine Network. *Photochem Photobiol* 63:397-400, 1996.
21. **Takashima A**, Bergstresser PR: Cytokine-mediated communication by keratinocytes and Langerhans cells with dendritic epidermal T cells. *Seminars in Immunology* 8:333-339, 1996.
22. Bergstresser PR, Elmetts CA, **Takashima A**, Mukhtar H: Photocarcinogenesis. *Photodermatology, Photoimmunology & Photomedicine* 11:181-184, 1996.

23. Ariizumi K, Bergstresser PR, **Takashima A**: Subtractive cDNA cloning: A new approach to understanding dendritic cell biology, in Dendritic Cells in Fundamental and Clinical Immunology, Ed. Ricchiardi-Castagnoli P, Plenum Publishing Company Ltd., London, 1997.
24. Bergstresser PR, Kitajima T, Xu S, Ariizumi K, **Takashima A**: T cell-mediated terminal maturation of dendritic cells, in Dendritic Cells in Fundamental and Clinical Immunology, Ed. Ricchiardi-Castagnoli P, Plenum Publishing, New York. p. 449-454, 1997.
25. **Takashima A**, Kitajima T: T cell mediated terminal maturation of dendritic cells, a critical transition into fully potent antigen presenting cells. *Pathologie Biologie* 46:53-60, 1998.
26. **Takashima A**: Preparation and Isolation of Cells: Preparing Fibroblasts, in Current Protocols in Cell Biology, Eds. Bonifacino JS, Dasso M, Harford JB, Lippincott-Schwartz J, Yamada KM, John Wiley & Sons, Inc., New York, 1999.
27. Kitajima T, **Takashima A**: Langerhans cell responses to ultraviolet B radiation. *J Dermatol Sci* 19:153-160, 1999.
28. Matsue H, **Takashima A**: Apoptosis in dendritic cell biology. *J Dermatol Sci* 20:159-171, 1999.
29. Morita A, **Takashima A**: Roles of Langerhans cells in genetic immunization. *J Dermatol Sci* 20:39-52 1999.
30. **Takashima A**, Bergstresser PR: Impact of UVB radiation on Langerhans cells: in vitro studies using XS 52 cell line, in Biologic Effects of Light 1998. Eds. M.F. Holick & EG Jung, Kluwer Academic Publishers, Boston. 181-190
31. **Takashima A**, Morita A: Dendritic cells in genetic immunization. *J Leuko Biology* 66:350-356, 1999.
32. Matsue M, Morita A, Matsue K, **Takashima A**: New technologies toward dendritic cell-based cancer immunotherapies. *J Dermatol* 26:757-763. 1999.
33. **Takashima A**, Mummert ME, Kitajima T, Matsue H: New technologies to prevent and treat contact hypersensitivity responses. *Ann NY Acad Sci* 919:205-213, 2000.
34. **Takashima A**, Bergstresser PR: Derivation of dendritic cell lines from mouse skin, in Dendritic Cell Protocols. Eds. Robinson S, Stagg A., Humana Press, New Jersey. 243-254, 2001.
35. **Takashima A**, Matsue H: Antigen presentation and biology of dendritic cells, in Immune Mechanics in Cutaneous Disease, Second Edition. Eds. Kupper TS, Norris DA: Marcel Dekker, Inc., New York. (in press) 2002.
36. **Takashima A**, Matsue H: Development and testing of dendritic cell lines, in Dendritic Cells: Biology and Clinical Applications, 2nd Edition. Eds. Lotze MT, Thomson AW: Academic Press Ltd., London, UK. 165-178, 2001.
37. Kumamoto T, Morita A, **Takashima A**: Recent advances in dendritic cell vaccines for cancer treatment. 28:658-662, *J Dermatol* 2001.
38. Matsue H, Kusuhara M, Matsue K, **Takashima A**: Dendritic Cell-Based Immunoregulatory Strategies. *Intl Arch Allergy Immunol* 127:251-258, 2002.

39. **Takashima A**, Matsue H, Kumamoto T, Mizumoto N, Morita A, Mummert M: Dendritic cells as a target for therapeutic intervention of contact hypersensitivity, in Immune Mechanisms in Allergic Contact Dermatitis. Eds. Cavani, A, Landes Bioscience, Georgetown, TX. 128-135, 2004.
40. Mizumoto N, **Takashima A**: CD1a and langerin: acting as more than Langerhans cell markers. *J Clin Invest*, 113:658-660, 2004.
41. Wilgus M-L, Adcock PA, **Takashima A**: Volume, trend, and citation analyses of skin related publications from 1966 to 2003. *J Dermatol Sci* (in press) 2005.